# **WEST Search History**

Hide Items Restore Clear Cancel

DATE: Thursday, November 15, 2007

Hide? Set Name Query

**Hit Count** 

DB=USPT; PLUR=YES; OP=ADJ

(546/219.ccls. or 514/328.ccls.) and (depression or anxiety or apnoea or migraine) L1

40

**END OF SEARCH HISTORY** 

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=> .s C19 H28 N2 O3/mf
          1376 C19 H28 N2 O3/MF
=> s 14 and piperidin?
       1236574 PIPERIDIN?
           277 L4 AND PIPERIDIN?
1.5
=> s 15 and piperidinedione
          4873 PIPERIDINEDIONE
             4 L5 AND PIPERIDINEDIONE
L6
=> d 1-3
     ANSWER 1 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN
L6
RN
     732209-36-8 REGISTRY
ED
     Entered STN: 24 Aug 2004
     2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-
CN
     4,4-dimethyl-, (+)- (CA INDEX NAME)
FS
     STEREOSEARCH
MF
     C19 H28 N2 O3
CI
     COM
SR
     CA
Rotation (+).
          Me
            Me
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  HN
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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
     ANSWER 2 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN
Lб
RN
     117576-37-1 REGISTRY
ED
     Entered STN: 18 Nov 1988
CN
     2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-
     4,4-dimethyl-, (-)- (CA INDEX NAME)
FS
     STEREOSEARCH
     C19 H28 N2 O3
MF
CI
     COM
SR
     CA
LC
     STN Files:
                  BEILSTEIN*, CA, CAPLUS, USPATFULL
         (*File contains numerically searchable property data)
Rotation (-).
```

### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

6 REFERENCES IN FILE CA (1907 TO DATE)

6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN

RN 117539-18-1 REGISTRY

ED Entered STN: 11 Nov 1988

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,5-dimethyl- (9CI) (CA INDEX NAME)

MF C19 H28 N2 O3

SR CA

LC STN Files: CA, CAPLUS

### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

## => FILE REG

COST IN U.S. DOLLARS

SINCE FILE TOTAL

ENTRY SESSION

32.10 40.34

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 11:02:53 ON 15 NOV 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 14 NOV 2007 HIGHEST RN 953817-57-7 DICTIONARY FILE UPDATES: 14 NOV 2007 HIGHEST RN 953817-57-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> STR 732209-36-8

: END

L7 STRUCTURE CREATED

=> S L7 FAM FUL

FULL SEARCH INITIATED 11:02:56 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 20 TO ITERATE

100.0% PROCESSED 20 ITERATIONS 13 ANSWERS

SEARCH TIME: 00.00.01

L8 13 SEA FAM FUL L7

=>

=> D SCAN

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-, sulfate (1:1)

MF C19 H28 N2 O3 . H2 O4 S

CM 1

CM 2

### HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):12

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1H-1,4-Benzodiazepine-3-carboxylic acid, 7-chloro-2,3-dihydro-2-oxo-5phenyl-, monopotassium salt, compd. with potassium hydroxide (K(OH))
 (1:1), mixt. with 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-2,6-piperidinedione (9CI)

MF C19 H28 N2 O3 . C16 H11 C1 N2 O3 . H K O . K

CI MXS

CM 1

CM 2

CM 3

$$HO_2C$$
 $N$ 
 $Ph$ 
 $C1$ 

K

CM 4

к-он

Rotation (+).

# \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-, (-)-

MF C19 H28 N2 O3

CI COM

Rotation (-).

# \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-, monohydrochloride, (+)- (9CI)

MF C19 H28 N2 O3 . Cl H

Rotation (+).

# ● HCl

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Naphthalenecarboxylic acid, 4,4'-methylenebis[3-hydroxy-, compd. with 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-2,6-piperidinedione (1:1) (9CI)

MF C23 H16 O6 . C19 H28 N2 O3

CM 1

CM 2

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-, monohydrochloride, mixt. with 7-chloro-1,3-dihydro-1-methyl-5phenyl-2H-1,4-benzodiazepin-2-one (9CI)

MF C19 H28 N2 O3 . C16 H13 Cl N2 O . Cl H

CI MXS

● HCl

CM 2

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-

MF C19 H28 N2 O3

CI COM

# \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-, hydrochloride (9CI)

MF C19 H28 N2 O3 .  $\times$  Cl H

# •x HCl

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-, monohydrochloride, (-)- (9CI)

MF C19 H28 N2 O3 . Cl H

Rotation (-).

# ● HCl

CM 1

Rotation (-).

CM 2

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-, monohydrochloride, mixt. with 7-chloro-N-methyl-5-phenyl-3H-1,4-benzodiazepin-2-amine 4-oxide, monohydrochloride (9CI)

MF C19 H28 N2 O3 . C16 H14 Cl N3 O . 2 Cl H

CI MXS

CM 1

HCl

CM 2

● HCl

L8 13 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-, hydrochloride (1:1)

MF C19 H28 N2 O3 . C1 H

CI COM

HCl

## ALL ANSWERS HAVE BEEN SCANNED

=> FILE REG

COST IN U.S. DOLLARS

SINCE FILE TOTAL

ENTRY SESSION

FULL ESTIMATED COST 68.15 108.49

FILE 'REGISTRY' ENTERED AT 11:04:17 ON 15 NOV 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES: 14 NOV 2007 HIGHEST RN 953817-57-7 DICTIONARY FILE UPDATES: 14 NOV 2007 HIGHEST RN 953817-57-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

13 ANSWERS

http://www.cas.org/support/stngen/stndoc/properties.html

=> STR 117576-37-1

WARNING. STEREO DATA NOT INCLUDED IN MODEL (NOT SEARCHABLE): END

L9 STRUCTURE CREATED

=> S L9 FAM FUL

FULL SEARCH INITIATED 11:04:21 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 20 TO ITERATE

100.0% PROCESSED 20 ITERATIONS

SEARCH TIME: 00.00.01

L10 13 SEA FAM FUL L9

(FILE 'HOME' ENTERED AT 10:55:56 ON 15 NOV 2007)

FILE 'REGISTRY' ENTERED AT 10:57:19 ON 15 NOV 2007 L1 1 S AGN 2979/CN

FILE 'CAPLUS' ENTERED AT 10:57:57 ON 15 NOV 2007

FILE 'REGISTRY' ENTERED AT 10:58:12 ON 15 NOV 2007

L2 1 S 53873-28-2 L3 1 S 117539-17-0

L4 1376 S C19 H28 N2 O3/MF

L5 277 S L4 AND PIPERIDIN?

L6 4 S L5 AND PIPERIDINEDIONE

FILE 'REGISTRY' ENTERED AT 11:02:53 ON 15 NOV 2007

STR 732209-36-8

L8 13 S L7 FAM FUL

FILE 'REGISTRY' ENTERED AT 11:04:17 ON 15 NOV 2007

L9 STR 117576-37-1

L10 13 S L9 FAM FUL

=> fil caplus

L7

COST IN U.S. DOLLARS

SINCE FILE TOTAL

ENTRY SESSION

FULL ESTIMATED COST 68.15 176.64

FILE 'CAPLUS' ENTERED AT 11:05:30 ON 15 NOV 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 15 Nov 2007 VOL 147 ISS 21 FILE LAST UPDATED: 14 Nov 2007 (20071114/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s 110

L11 19 L10

=> s l1

L12 15 L1

=> s 111 not 112

L13 4 L11 NOT L12

=> d bib abs hitstr 1-4

L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

```
2004:182707 CAPLUS
ΝA
DN
     140:210809
     Piperidin-2,6-dione pamoate salts for the treatment of stress-related
TI
     affective disorders, and pharmaceutical compositions containing them
IN
     Wermuth, Camille Georges
PA
     Prestwick Pharmaceuticals, Inc., USA
SO
     PCT Int. Appl., 21 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
                                            _____
                                                                    _____
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                         _ _ _ _
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                                                                    20030818
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     WO 2004017970
                          A1
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
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             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
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PRAI GB 2002-19639
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                                20020822
     WO 2003-IB3698
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                          W
OS
     MARPAT 140:210809
```

$$R^{2}$$
 $(CH_{3})_{2}N-(CH_{2})_{n}$ 
 $N$ 

GI

AB Pamoate salts of certain 3-phenyl-3-dimethylaminoalkyl-4,4dimethylpiperidin-2,6-diones,(I) (R1 = MeO, EthO, OH; R2 = MeO, EthO, OH; n = 2, 3) and pharmacol. acceptable solvates thereof are devoid of the weight loss and hepatocyte changes in the rat which limited to marginally effective levels the permitted clin. doses of the corresponding

I

hydrochlorides in the treatment or prophylaxis of stress-related affective disorders such as anxiety, depression, migraine and sleep apnea. The preferred pamoate salts are 3(3,5dimethoxyphenyl)-3-(3-dimethylaminopropyl)-4,4-dimethylpiperidine-2,6-dione pamoate and, especially, 3(3-methoxyphenyl)-3-(3-dimethylaminopropyl)-4,4-dimethylpiperidine2,6-dione pamoate.

IT 666175-71-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(piperidin-2,6-dione pamoate salts for treatment of stress-related affective disorders, and pharmaceutical compns. containing them)

RN 666175-71-9 CAPLUS

2-Naphthalenecarboxylic acid, 4,4'-methylenebis[3-hydroxy-, compd. with 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-2,6-piperidinedione (1:1) (9CI) (CA INDEX NAME)

CM 1

CN

CRN 53873-21-5 CMF C19 H28 N2 O3

CM 2

CRN 130-85-8 CMF C23 H16 O6

IT 666175-73-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(piperidin-2,6-dione pamoate salts for treatment of stress-related affective disorders, and pharmaceutical compns. containing them)
666175-73-1 CAPLUS

RN 666175-73-1 CAPLUS
CN 2-Naphthalenecarboxylic acid, 4,4'-methylenebis[3-hydroxy-, compd. with (-)-3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-2,6-piperidinedione (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 117576-37-1 CMF C19 H28 N2 O3

Rotation (-).

CM 2

CRN 130-85-8 CMF C23 H16 O6

IT 500350-77-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(piperidin-2,6-dione pamoate salts for treatment of stress-related affective disorders, and pharmaceutical compns. containing them)

RN 500350-77-6 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 53873-21-5 CMF C19 H28 N2 O3

CM 2

CRN 7664-93-9 CMF H2 O4 S

#### RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

2003:174547 CAPLUS AN

DN 138:204953

Preparation of piperidine-2,6-dione bisulfate salts useful for the ΤI treatment of stress-related affective disorders

Gittos, Maurice Ward IN

PA Fr.

SO Brit. UK Pat. Appl., 26 pp.

CODEN: BAXXDU

DT Patent

English LA

FAN.	CNT	1																
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												TR,				-	•	•
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	AT 347891	T	20070115	AT 2002-755226	20020822
	ES 2275898	Т3	20070616	ES 2002-2755226	20020822
	MX 2004PA01777	A	20041122	MX 2004-PA1777	20040225
	US 2004249159	A1	20041209	US 2004-486925	20040225
	US 7189742	B2	20070313		
	IN 2004MN00151	Α	20050624	IN 2004-MN151	20040227
PRAI	GB 2001-20821	Α	20010828		
	WO 2002-GB3869	W	20020822		
os	MARPAT 138:204953				
GT					

$$R^{1}$$
 $Me Me$ 
 $R^{2}$ 
 $Me_{2}N(CH_{2})_{n}$ 
 $Me_{3}N(CH_{2})_{n}$ 
 $Me_{4}N(CH_{2})_{n}$ 
 $Me_{5}N(CH_{2})_{n}$ 

Ι

Title compds. [I; R1 = MeO, EtO, OH; R2 = H, R1; n = 2, 3], were prepared Thus, a cooled solution of H2SO4 in EtOH was mixed into 3-(3-methoxyphenyl)-3-(3-dimethylaminopropyl)-4,4-dimethylpiperidine-2,6-dione (AGN 2979) in EtOH followed by removal of solvent under reduced pressure and recrystn. from EtOH to give the bisulfate (II). II at 65 mg every 2 days in a 90 kg human male eliminated episodes of obstructive sleep apnea. II drug formulations are given. I are devoid of the weight loss and hepatocyte changes in the rat which limited to marginally effective levels the permitted clin. doses of the corresponding hydrochlorides in the treatment or prophylaxis of stress-related affective disorders such as anxiety, depression, migraine and sleep apnea.

IT 500350-77-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidine-2,6-dione bisulfate salts useful for the treatment of stress-related affective disorders)

RN 500350-77-6 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-, sulfate (1:1) (CA INDEX NAME)

CM 1

CRN 53873-21-5 CMF C19 H28 N2 O3

#### THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN L13

1989:580731 CAPLUS AN

DN 111:180731

Anxiolytic pharmaceuticals containing 3-phenyl-3-(aminoalkyl)-4-methyl-2,6-TI dioxopiperidine derivatives

IN Costall, Brenda

National Research Development Corp., UK PA

Brit. UK Pat. Appl., 45 pp. SO

CODEN: BAXXDU

DT Patent

LA English

FAN. CNT 1

PAN.C	NI T				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2206491	A	19890111	GB 1988-16214	19880707
	GB 2206491	В	19910123		
	EP 299680	A2	19890118	EP 1988-306208	19880707
	EP 299680	A3	19890726		
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	DK 8803826	Α	19890111	DK 1988-3826	19880708
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	ZA 8804986	Α	19900328	ZA 1988-4986	19880711
PRAI	GB 1987-16338	Α	19870710		
os	MARPAT 111:180731				

GI

$$R^{5}$$
 Me  $R^{6}$   $R^{7}$   $R^{7}$ 

AΒ 3-Phenyl-3-aminoalkyl-4-methyl-2,6-dioxopiperidine derivs. (I; R1 = H, alkyl; n = 1, 2; R2 = H, Me, provided that one of R2 = H if n = 2; R3 = H, alkyl; R4 = alkyl; R5, R6 = H, Me; m = 0-3; each Y is in a meta or para position and represents OH, alkoxy, alkyl, hydroxyalkyl, halo, CF3, provided that OH and alkoxy are not in the para position) or their salts antagonize anxiogenesis associated with the withdrawal of addictive drugs, especially alc., nicotine, and cocaine. Tablets contained 3-(3'-methoxyphenyl)-

3-(3"-N,N-dimethylaminopropyl)-4,4-dimethyl-2,6-dioxopiperidine (II)

(base) 1, lactose 51.5, dried maize starch 45, and Mg stearate 1.5 mg/tablet. Mice were exposed to 8% alc. in the drinking water and during alc. withdrawal they received 10 mg diazepam/kg i.p. or 0.5 mg II/kg i.p. The mice were previously kept in a darkened box and during testing placed in a test area with white and black areas; during alc. intake the mice showed anxiolysis characterized by increased exploratory behavior in the white section and when the alc. was withdrawn the reverse profile was observed Both diazepam and II not only reversed anxiogenesis but actually led to anxiolysis; both appeared to be equieffective to combat anxiogenesis in alc. withdrawal, but II was more potent and devoid of the initial sedative action seen on treatment with diazepam. Both II and diazepam antagonized anxiogenesis in cocaine withdrawal in mice or in nicotine withdrawal in marmosets. I had no action on benzodiazepine receptors.

IT 53873-21-5 117576-37-1 123323-80-8

RL: BIOL (Biological study)

(as anxiolytic, for treatment of anxiogenesis associated with addictive drug withdrawal)

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

RN 117576-37-1 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-, (-)- (CA INDEX NAME)

Rotation (-).

RN 123323-80-8 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

Me (CH<sub>2</sub>) 
$$_3$$
 – NMe<sub>2</sub>

### ●x HCl

os

GI

MARPAT 111:146823

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN 1989:546823 CAPLUS AN111:146823 DN Phenyl-3-aminoalkyl-4-methyl-2,6-dioxopiperidine derivatives and their use TI as antipsychotic agents IN Costall, Brenda PΑ National Research Development Corp., UK SO Eur. Pat. Appl., 14 pp. CODEN: EPXXDW DT Patent LA English FAN.CNT 1 DATE PATENT NO. KIND DATE APPLICATION NO. -------------------\_\_\_\_\_ 19890111 EP 1988-306207 19880707 PΙ EP 298738 A2 EP 298738 Α3 19890809 EP 298738 B1 19920930 R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE GB 2206490 Α 19890111 GB 1988-16213 19880707 GB 2206490 В 19910918 AT 81003 Т 19921015 AT 1988-306207 19880707 DK 8803825 19890111 DK 1988-3825 19880708 Α DK 170360 B1 19950814 AU 8818861 Α 19890127 AU 1988-18861 19880708 AU 606701 B2 19910214 ZA 8804937 Α 19900328 ZA 1988-4937 19880708 19890309 JP 1988-173620 19880711 JP 01063516 A US 1988-217450 19880711 US 4877800 Α 19891031 CA 1988-571649 19880711 CA 1328077 С 19940329 PRAI GB 1987-16337 A 19870710 EP 1988-306207 19880707

Α

I

Phenyl-3-aminoalkyl-4-methyl-2,6-dioxopiperidine derivs. (I; R1, R3 = H, AB alkyl; n = 1,2; R2 = H, Me, provided that R2 = H when n = 2; R4 = alkyl; R5,R6 = H, Me; m = 0-3; Y is in a meta- or para-position; Y = OH, alkoxy, alkyl, hydroxyalkyl, halo, CF3, provided that OH and alkoxy are not in the para-position) or its salts are used for the manufacture of pharmaceuticals used in the treatment of psychosis. Hyperactivity was induced in rats via sterotaxic surgery, i.e. implantation of cannulae for intracerebral infusion of dopamine into the center of the nucleus accumbens and 25 µg dopamine was thus infused over a 24 h time period. Dopamine-induced hyperactivity occurred in a biphasic pattern between days 2-5 and 9-12 of treatment and could be antagonized with 0.01-10 mg/kg i.p. doses of 3-(3'-methoxyphenyl)-3-(3''-N, N-dimethylaminopropyl)-4,4-dimethyl-2,6dioxopiperidine (II); a lower dose of II (0.00001 mg/kg) controlled the 2nd peak but prevented control of the 1st peak. After withdrawal of II and dopamine a rebound of hyperactivity was not observed; persistent or excessive motor depression was not observed either with II during treatment. Fluphenazine at a 0.025-0.05 mg/kg dose was also effective in controlling dopamine-induced hyperactivity, however, after withdrawal, a rebound activity was observed Tablets contained II 1, lactose 51.5, dried maize starch 45, and Mg stearate 1.5 mg each.

IT 53873-21-5 117576-37-1 RL: BIOL (Biological study) (antipsychotic agent)

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

RN 117576-37-1 CAPLUS
CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl-, (-)- (CA INDEX NAME)

Rotation (-).

```
666175-74-2 or 53873-21-5 or 92519-16-9 or
                                                      117576-37-1
             1 666175-74-2
                  (666175-74-2/RN)
             1 53873-21-5
                 (53873-21-5/RN)
             1 92519-16-9
                  (92519-16-9/RN)
             1 117576-37-1
                  (117576-37-1/RN)
L4
             4 666175-74-2 OR 53873-21-5 OR 92519-16-9 OR
                                                                117576-37-1
=> d 14
L4
     ANSWER 1 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN
     666175-74-2 REGISTRY
RN
ED
     Entered STN: 22 Mar 2004
CN
     2,6-Piperidinedione, 3-(3,5-dimethoxyphenyl)-3-[3-(dimethylamino)propyl]-
     4,4-dimethyl-, (-)- (CA INDEX NAME)
FS
     STEREOSEARCH
MF
     C20 H30 N2 O4
CI
     COM
SR
     CA
LC
     STN Files:
                  CA, CAPLUS
Rotation (-).
          Me
            Me
                    NMe2
  HN
             (CH<sub>2</sub>) 3
 MeO
                OMe
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
=> d 14 2-4
L4
     ANSWER 2 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN
RN
     117576-37-1 REGISTRY
ED
     Entered STN: 18 Nov 1988
     2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-
CN
     dimethyl-, (-)- (CA INDEX NAME)
FS
     STEREOSEARCH
MF
     C19 H28 N2 O3
CI
     COM
SR
     CA
LC
                  BEILSTEIN*, CA, CAPLUS, USPATFULL
     STN Files:
         (*File contains numerically searchable property data)
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Rotation (-).

### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

- 6 REFERENCES IN FILE CA (1907 TO DATE)
- 6 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L4 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN
- RN 92519-16-9 REGISTRY
- ED Entered STN: 17 Dec 1984
- CN 2,6-Piperidinedione, 3-(3,5-dimethoxyphenyl)-3-[3-(dimethylamino)propyl]-4,4-dimethyl- (CA INDEX NAME)
- MF C20 H30 N2 O4
- CI COM
- LC STN Files: CA, CAPLUS, USPATZ, USPATFULL

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# \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

- 4 REFERENCES IN FILE CA (1907 TO DATE)
- 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L4 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN
- RN 53873-21-5 REGISTRY
- ED Entered STN: 16 Nov 1984
- CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

### OTHER NAMES:

- CN 3-[3-(Dimethylamino)propyl]-3-(m-methoxyphenyl)-4,4-dimethyl-2,6-piperidinedione
- DR 117539-16-9
- MF C19 H28 N2 O3
- CI COM
- LC STN Files: BEILSTEIN\*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, MEDLINE,

PHAR, PROUSDDR, RTECS\*, TOXCENTER, USPATFULL (\*File contains numerically searchable property data)

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

- 11 REFERENCES IN FILE CA (1907 TO DATE)
- 11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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 => s 14 
 L5
              12 L4
 => s 15 and weight
          150877 WEIGHT
               0 L5 AND WEIGHT
 L6
 => d bib abs hitstr 15 1-12
      ANSWER 1 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
 AN
      2007:329586 CAPLUS
 DN
      146:330838
      4,4-Dimethylpiperidine-2,6-dione derivatives for use in the treatment of
 TI
      hypertension
 IN
      Gittos, Maurice Ward
      Prestwick Pharmaceuticals, Inc., USA
 PA
 SO
      PCT Int. Appl., 20pp.
      CODEN: PIXXD2
 DT
      Patent
 LΑ
      English
 FAN.CNT 1
      PATENT NO.
                                    DATE
                            KIND
                                                APPLICATION NO.
                                                                         DATE
       ______
                            ____
                                    _____
                                                -----
 PΙ
      WO 2007031737
                             A1
                                    20070322
                                                WO 2006-GB3379
                                                                         20060913
               AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
               CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
               GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
               KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
               MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
               RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
               UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
           RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
               IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
               KG, KZ, MD, RU, TJ, TM
 PRAI GB 2005-18763
                             Α
                                    20050914
 OS
      MARPAT 146:330838
 AB
      Hypertension is treated with certain 3-phenyl-3-dimethylaminoalkyl-4,4-
      dimethylpiperidin-2,6-diones. The preferred compds. are
       3(3,5-dimethoxyphenyl)-3- (3-dimethylaminopropyl)-4,4-dimethylpiperidine-
      2,6-dione salts and, especially, 3(3-methoxyphenyl)-3-(3-dimethylaminopropyl)-
       4,4-dimethylpiperidine-2,6-dione salts.
 IT
       53873-21-5 92519-16-9 117576-37-1
       666175-74-2
       RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
       (Biological study); USES (Uses)
          (dimethylpiperidinedione derivs. for treatment of hypertension)
 RN
       53873-21-5 CAPLUS
 CN
       2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-
       dimethyl- (CA INDEX NAME)
          Me
```

RN 92519-16-9 CAPLUS

CN 2,6-Piperidinedione, 3-(3,5-dimethoxyphenyl)-3-[3-(dimethylamino)propyl]-4,4-dimethyl- (CA INDEX NAME)

RN 117576-37-1 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-, (-)- (CA INDEX NAME)

Rotation (-).

RN 666175-74-2 CAPLUS

CN 2,6-Piperidinedione, 3-(3,5-dimethoxyphenyl)-3-[3-(dimethylamino)propyl]-4,4-dimethyl-, (-)- (CA INDEX NAME)

Rotation (-).

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN AN 2003:174547 CAPLUS

```
DN
      138:204953
. TI
      Preparation of piperidine-2,6-dione bisulfate salts useful for the
      treatment of stress-related affective disorders
IN
      Gittos, Maurice Ward
PA
SO
      Brit. UK Pat. Appl., 26 pp.
      CODEN: BAXXDU
DT
      Patent
      English
LΑ
FAN.CNT 1
      PATENT NO.
                          KIND
                                  DATE
                                              APPLICATION NO.
                                                                       DATE
 PΙ
      GB 2379216
                            Α
                                  20030305
                                              GB 2001-20821
                                                                       20010828
      CA 2459009
                            Α1
                                  20030313
                                              CA 2002-2459009
                                                                       20020822
      WO 2003020275
                           A1
                                  20030313
                                              WO 2002-GB3869
                                                                      20020822
              AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
              UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
              CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
              NE, SN, TD, TG
      AU 2002321522
                            A1
                                  20030318
                                              AU 2002-321522
                                                                      20020822
      EP 1420788
                            A1
                                  20040526
                                              EP 2002-755226
                                                                      20020822
      EP 1420788
                            В1
                                  20061213
              AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
      BR 2002012175
                                              BR 2002-12175
                            Α
                                  20040720
                                                                       20020822
      CN 1549715
                            Α
                                  20041124
                                              CN 2002-816912
                                                                      20020822
      JP 2005502677
                            Т
                                  20050127
                                              JP 2003-524582
                                                                      20020822
      NZ 531345
                            Α
                                  20050729
                                              NZ 2002-531345
                                                                      20020822
      AT 347891
                            Т
                                  20070115
                                              AT 2002-755226
                                                                      20020822
      ES 2275898
                            Т3
                                  20070616
                                              ES 2002-2755226
                                                                      20020822
      MX 2004PA01777
                            Α
                                  20041122
                                              MX 2004-PA1777
                                                                      20040225
      US 2004249159
                            A1
                                  20041209
                                              US 2004-486925
                                                                      20040225
                            B2
      US 7189742
                                  20070313
      IN 2004MN00151
                            Α
                                  20050624
                                              IN 2004-MN151
                                                                      20040227
 PRAI GB 2001-20821
                            Α
                                  20010828
```

20020822

$$R^{1}$$
 $R^{2}$ 
 $Me_{2}N(CH_{2})_{n}$ 
 $N$ 
 $H$ 

WO 2002-GB3869

MARPAT 138:204953

os

GΙ

W

Ι

AB Title compds. [I; R1 = MeO, EtO, OH; R2 = H, R1; n = 2, 3], were prepared Thus, a cooled solution of H2SO4 in EtOH was mixed into 3-(3-methoxyphenyl)-3-(3-dimethylaminopropyl)-4,4-dimethylpiperidine-2,6-dione (AGN 2979) in EtOH followed by removal of solvent under reduced pressure and recrystn.

from EtOH to give the bisulfate (II). II at 65 mg every 2 days in a 90 kg human male eliminated episodes of obstructive sleep apnea. II drug formulations are given. I are devoid of the weight loss and hepatocyte changes in the rat which limited to marginally effective levels the permitted clin. doses of the corresponding hydrochlorides in the treatment or prophylaxis of stress-related affective disorders such as anxiety, depression, migraine and sleep apnea.

IT 92519-16-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperidine-2,6-dione bisulfate salts useful for the treatment of stress-related affective disorders)

RN 92519-16-9 CAPLUS

CN 2,6-Piperidinedione, 3-(3,5-dimethoxyphenyl)-3-[3-(dimethylamino)propyl]-4,4-dimethyl- (CA INDEX NAME)

Me (CH<sub>2</sub>) 
$$_3$$
 - NMe<sub>2</sub>

Me OMe

# RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1992:106095 CAPLUS

DN 116:106095

TI Process for preparation of 3-aryl-3-aminoalkyl-2,6-dioxohexahydropyridines

IN Dygos, John Henry; McLaughlin, Kathleen Therese; Ng, John Sau Hoi; Paul,
 Kalidas

PA G.D. Searle and Co., USA

SO Eur. Pat. Appl., 15 pp. CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	J11				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	EP 448972	A2	19911002	EP 1991-102833	19910226
	EP 448972	A3	19920506		
	. R: AT, BE, CH,	DE, DK	, ES, FR, G	BB, GR, IT, LI, LU, NL,	SE
	US 5104990	A	19920414	US 1990-486027	19900227
	CA 2036968	A1	19910828	CA 1991-2036968	19910225
	JP 04211657	Α	19920803	JP 1991-30929	19910226
	JP 06094460	В	19941124		
	US 5220019	Α	19930615	US 1992-859189	19920327
PRAI	US 1990-486027	Α	19900227		
os	CASREACT 116:106095	; MARPA	T 116:10609	95	
GI					•

AB A process is disclosed for the preparation of title compds. I [A = straight or branched C2-6 alkalene; R,R1 = C1-10 alkyl; Ar = heterocyclyl, (substituted) aryl] and particularly 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-2,6-piperidinedione monohydrochloride (II), which is useful as an antidepressant. Thus, 6.58 Kg [(dimethylamino)propyl]methoxybenzeneacetonitrile, preparation given from 3-MeOC6H4CH2CN and C1(CH2)3NMe2.HCl, was treated with 11.89 Kg of (Me2CH)2CHLi and then 6.25 Kg Me2C:C(CO2Et)2 in THF-heptane to give 84.69% 3-MeOC6H4C(CN)[CMe2CH(CO2Et2](CH2)3NMe2.HCl. Hydrolysis of the latter compound in refluxing 96% H2SO4 and then treatment with 29% NH4OH followed by 36% aq HCl in EtOH gave 83.5% II.

IT 53873-21-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

L5 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1991:609 CAPLUS

DN 114:609

TI Low-dosage anxiolytic compositions containing dioxopiperidine derivatives

IN Costall, Brenda

PA National Research Development Corp., UK

SO S. African, 56 pp.

CODEN: SFXXAB

DT Patent

LA English

FAN.CNT 1

T LTIA .	TAN: CNI I									
	PATENT NO.	KIND	DATE	APPLICATION NO.	· DATE					
PI	ZA 8804938	Α	19900328	ZA 1988-4938	19880708					
	IL 87059	Α	19921201	IL 1988-87059	19880710					
PRAI	GB 1987-16340	Α	19870710		,					
os	MARPAT 114:609									
GT .										

Dioxopiperidine derivs. I [R1 = H, C1-4 alkyl; R2 = H, Me, provided that one R2 = H when n = 2; n = 1,2; R3 = H, C1-2 alkyl; R4 = C1-2 alkyl; R5, R6 = H, Me; m = 0-3; Y = OH, C1-2 alkoxy, C1-2 (hydroxy)alkyl, halo, trifluoromethyl in a meta or para position, provided that OH and alkoxy are not in the para position] or pharmaceutically acceptable salts are low-dosage anxiolytics; pharmaceutical compns. comprise I at 10-7-10-1 mg/unit dose. 3-(3'-Methoxyphenyl)-3-(3''-N,N-dimethylethylaminopropyl)-4,4-dimethyl-2,6-dioxopiperidine (II) at 0.00001-100.0 mg/kg s.c. showed anxiolytic activity in male albino BKW mice. The effect was achieved in the absence of sedation. Tablets comprise II 0.1, lactose 51.5, maize starch 45, and Mg stearate 1.5 mg/tablet.

IT 53873-21-5 117576-37-1

RL: BIOL (Biological study)
 (low-dosage anxiolytic)

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

RN 117576-37-1 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-, (-)- (CA INDEX NAME)

Rotation (-).

AN 1989:580731 CAPLUS

DN 111:180731

TI Anxiolytic pharmaceuticals containing 3-phenyl-3-(aminoalkyl)-4-methyl-2,6dioxopiperidine derivatives

IN Costall, Brenda

National Research Development Corp., UK PA

SO Brit. UK Pat. Appl., 45 pp. CODEN: BAXXDU

DTPatent

English LА

FAN.	CNT 1				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	GB 2206491	Α	19890111	GB 1988-16214	19880707
	GB 2206491	В	19910123		
	EP 299680	A2	19890118	EP 1988-306208	19880707
	EP 299680	A3	19890726		
	R: AT, BE, CH,	DE, FR	, GB, IT, LI	, LU, NL, SE	
	DK 8803826	Α	19890111	DK 1988-3826	19880708
	AU 8818862	Α	19890112	AU 1988-18862	19880708
	AU 609496	B2	19910502		
	JP 01063517	Α	19890309	JP 1988-173621	19880711
	ZA 8804986	Α	19900328	ZA 1988-4986	19880711
PRAI	GB 1987-16338	Α	19870710	•	,
os	MARPAT 111:180731				
GT				•	

$$R^{5}$$
 Me  $R^{6}$ 
 $R^{3}$  N (CH)  $n^{1}$  H2C N  $R^{1}$  R2

AB 3-Phenyl-3-aminoalkyl-4-methyl-2,6-dioxopiperidine derivs. (I; R1 = H, alkyl; n = 1, 2; R2 = H, Me, provided that one of R2 = H if n = 2; R3 = H, alkyl; R4 = alkyl; R5, R6 = H, Me; m = 0-3; each Y is in a meta or para position and represents OH, alkoxy, alkyl, hydroxyalkyl, halo, CF3, provided that OH and alkoxy are not in the para position) or their salts antagonize anxiogenesis associated with the withdrawal of addictive drugs, especially alc., nicotine, and cocaine. Tablets contained

3-(3'-methoxyphenyl)-3-(3"-N,N-dimethylaminopropyl)-4,4-dimethyl-2,6-dioxopiperidine (II) (base) 1, lactose 51.5, dried maize starch 45, and Mg stearate 1.5 mg/tablet. Mice were exposed to 8% alc. in the drinking water and during alc. withdrawal they received 10 mg diazepam/kg i.p. or 0.5 mg II/kg i.p. The mice were previously kept in a darkened box and during testing placed in a test area with white and black areas; during alc. intake the mice showed anxiolysis characterized by increased exploratory behavior in the white section and when the alc. was withdrawn the reverse profile was observed Both diazepam and II not only reversed anxiogenesis but actually led to anxiolysis; both appeared to be equieffective to combat anxiogenesis in alc. withdrawal, but II was more potent and devoid of the initial sedative action seen on treatment with diazepam. Both II and diazepam antagonized anxiogenesis in cocaine withdrawal in mice or in nicotine withdrawal in marmosets. I had no action on benzodiazepine receptors.

IT 53873-21-5 117576-37-1

RL: BIOL (Biological study)

(as anxiolytic, for treatment of anxiogenesis associated with addictive drug withdrawal)

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

RN 117576-37-1 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-, (-)- (CA INDEX NAME)

Rotation (-).

L5 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1989:546823 CAPLUS

DN 111:146823

TI Phenyl-3-aminoalkyl-4-methyl-2,6-dioxopiperidine derivatives and their use as antipsychotic agents

IN Costall, Brenda

PA National Research Development Corp., UK

SO Eur. Pat. Appl., 14 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
PI	EP 298738 EP 298738	A2 1989011 A3 1989080	9	19880707
	EP 298738 R: AT, BE, CH	B1 1992093 DE, FR, GB, IT	LI, LU, NL, SE	
	GB 2206490	A 1989011	•	19880707
	GB 2206490	B 1991091	.8	
	AT 81003	T 1992101	.5 AT 1988-306207	19880707
	DK 8803825	A 1989011	1 DK 1988-3825	19880708

	DK 170360	В1	19950814		
•	AU 8818861	Α	19890127	AU 1988-18861	19880708
	AU 606701	B2	19910214		
	ZA 8804937	Α	19900328	ZA 1988-4937	19880708
	JP 01063516	Α	19890309	JP 1988-173620	19880711
	US 4877800	Α	19891031	US 1988-217450	19880711
	CA 1328077	С	19940329	CA 1988-571649	<sup>.</sup> 19880711
PRAI	GB 1987-16337	Α	19870710		
	EP 1988-306207	Α	19880707		
os	MARPAT 111:146823				
GI					

AB Phenyl-3-aminoalkyl-4-methyl-2,6-dioxopiperidine derivs. (I; R1, R3 = H, alkyl; n = 1,2; R2 = H, Me, provided that R2 = H when n = 2; R4 = alkyl; R5, R6 = H, Me; m = 0-3; Y is in a meta- or para-position; Y = OH, alkoxy, alkyl, hydroxyalkyl, halo, CF3, provided that OH and alkoxy are not in the para-position) or its salts are used for the manufacture of pharmaceuticals used in the treatment of psychosis. Hyperactivity was induced in rats via sterotaxic surgery, i.e. implantation of cannulae for intracerebral infusion of dopamine into the center of the nucleus accumbens and 25 µg dopamine was thus infused over a 24 h time period. Dopamine-induced hyperactivity occurred in a biphasic pattern between days 2-5 and 9-12 of treatment and could be antagonized with 0.01-10 mg/kg i.p. doses of 3-(3'-methoxyphenyl)-3-(3''-N,N-dimethylaminopropyl)-4,4-dimethyl-2,6dioxopiperidine (II); a lower dose of II (0.00001 mg/kg) controlled the 2nd peak but prevented control of the 1st peak. After withdrawal of II and dopamine a rebound of hyperactivity was not observed; persistent or excessive motor depression was not observed either with II during treatment. Fluphenazine at a 0.025-0.05 mg/kg dose was also effective in controlling dopamine-induced hyperactivity, however, after withdrawal, a rebound activity was observed Tablets contained II 1, lactose 51.5, dried maize starch 45, and Mg stearate 1.5 mg each.

IT 53873-21-5 117576-37-1

RL: BIOL (Biological study) (antipsychotic agent)

Ι

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4dimethyl- (CA INDEX NAME)

RN 117576-37-1 CAPLUS

2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-CN dimethyl-, (-)- (CA INDEX NAME)

Rotation (-).

L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ΑN 1989:540496 CAPLUS

111:140496 DN

TI 2,6-Piperidinediones as analgesics

IN Roberts, Malcolm Henry Traffod

PΑ National Research Development Corp., UK

SO Eur. Pat. Appl., 22 pp.

CODEN: EPXXDW

DT Patent

English LΑ

FAN.	CNT 1				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
					<b></b>
ΡI	EP 295836	A2	19881221	EP 1988-305317	19880610
	EP 295836	A3	19890719		
	EP 295836	B1	19920902		
	R: AT, BE, CH,	DE, FR	, GB, IT, L	I, LU, NL, SE	
	GB 2205745	Α	19881221	GB 1988-13796	19880610
	GB 2205745	В	19900919		
	AT 80035	${f T}$	19920915	AT 1988-305317	19880610
	AU 8817676	Α	19881222	AU 1988-17676	19880614
	AU 606424	B2	19910207	•	
	US 4871750	Α	19891003	US 1988-206273	19880614
	DK 8803282	Α	19881217	DK 1988-3282	19880615
	ZA 8804275	Α	19890530	ZA 1988-4275	19880615
	JP 01016763	Α	19890120	JP 1988-149237	19880616
PRAI	GB 1987-14033	Α	19870616		
	GB 1987-14374	Α	19870619		
	EP 1988-305317	Α	19880610	•	
os	MARPAT 111:140496				
GI					

Phenyl-3-(aminoalkyl)-4-methyl-2,6-piperidinediones I (R1 = H, C1-4 alkyl; R2 = H, Me with one R2 = H when n = 2; R3 = H, Me, Et; R4 = Me, Et; R5, R6 = H, Me; Y = OH, MeO, EtO, Me, Et, HOCH2, hydroxyethyl, halo, CF3; n = 1, 2; m = 0-3 with each Y in a meta or para position) or their salts are useful as analgesics. Using the tail-flick latency test, (-)-3-(3-methoxyphenyl)-3-[3-(dimethylamino)propyl]-4,4-dimethyl-2,6-piperidinedione [(-)-II] injected into rats at 2 mg/kg had a strong analgesic effect with the peak response delayed until 20 min after the injection and baseline latencies were not recovered until 2 h after the injection; the potency was of the same order of magnitude as morphine with a similar time course of effect. Naloxone, known to block drug actions at opioid receptors, failed to reduce the potency of this compound Tablets contained II 50, lactose 51.5, dried corn starch 45, and Mg stearate 1.5 mg/tablet.

IT 53873-21-5 117576-37-1
RL: BIOL (Biological study)
(analgesic pharmaceuticals containing)

Ι

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

RN 117576-37-1 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-, (-)- (CA INDEX NAME)

Rotation (-).

L5 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1988:622491 CAPLUS

DN 109:222491

TI Anxiolytic compositions containing dioxopiperidine derivatives

IN Gittos, Maurice Ward; Costall, Brenda

PA National Research Development Corp., UK

SO Eur. Pat. Appl., 34 pp. CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 263594 EP 263594 EP 263594	A2 A3 B1	19880413 19890802 19920624	EP 1987-307860	19870904
	R: BE, CH, DE,	ES, FR	, GB, IT,	LI, LU, NL, SE	
	GB 2181346	Α	19870423	GB 1986-21577	19860908
	GB 2181346	В	19891004		
	GB 2196251	Α	19880427	GB 1987-20813	19870904
	GB 2196251	В	19900704		
	CA 1316112	C	19930413	CA 1987-546240	19870904
	DK 8704654	Α	19880309	DK 1987-4654	19870907
	AU 8778109	Α	19880310	AU 1987-78109	19870907
	AU 602716	B2	19901025		
	JP 63101361	Α	19880506	JP 1987-225124	19870908
	AU 9059784	Α	19901101	AU 1990-59784	19900724
PRAI		Α	19860908		
	GB 1987-16339	Α	19870710		
	GB 1985-22455	Α	19850911		
	GB 1986-3909	Α	19860217		
	GB 1986-3910	A	19860217		
	GB 1987-16359	Α	19870710		•
os GI	MARPAT 109:222491				

A pharmaceutical composition in unit dose form comprises, with a . AB pharmaceutically acceptable diluent or carrier, 10-7-10-1 mg/unit dose of 3-phenyl-3-aminoalkyl-4-methyl-2,6-dioxopiperidines I (R1 = H, C1-4 alkyl; n = 1,2; R2 = H, Me, provided that one R2 = H when n = 2; R3 = H, C1-2alkyl; R4 = C1-2 alkyl; R5, R6 = H, Me; m = 0-3; Y = OH, C1-2 alkoxy, C1-2alkyl, C1-2 hydroxyalkyl, halo, CF3, in meta or para position, provided that OH and alkoxy are not in para position) or pharmaceutically acceptable salts for treatment of anxiety. Native male albino BKW mice in an anti-anxiety test were administered 3(3'-methoxyphenyl)-3(3''-N,Ndimethylaminopropyl)-4,4-dimethyl-2,6-dioxopiperidine (II) in water by s.c. injection or diazepam in PEG and water by i.p. injection. II was as effective as diazepam and, in fact, was exceptionally potent (0.00001-100.0 mg/kg) and showed a dose range of 10 million (106). dose related effects of II contrasted with the all-or-none response of diazepam. A gelatin capsule formulation comprised II HCl 2.5 and talc 70 mg/capsule.

IT 53873-21-5 92519-16-9 117576-37-1 RL: BIOL (Biological study)

(anxiolytic)

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

RN 92519-16-9 CAPLUS

CN 2,6-Piperidinedione, 3-(3,5-dimethoxyphenyl)-3-[3-(dimethylamino)propyl]-4,4-dimethyl- (CA INDEX NAME)

RN 117576-37-1 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl-, (-)- (CA INDEX NAME)

Rotation (-).

L5 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1987:605181 CAPLUS

DN 107:205181

TI Use of dioxopiperidine derivatives in the treatment of anxiety, for the reduction of abnormally high brain levels of serotonin or 5-hydroxyindoleacetic acid, and in the treatment of bacterial or viral infections

IN Gittos, Maurice Ward

PA National Research Development Corp., UK

SO Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 2

GI

	PAT	TENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP	216555	A2 A3 B1	19891123	EP 1986-306920	19860908
		R: BE, CH, DE,	FR, GB	, IT, LI,	LU, NL, SE	
			A2		EP 1991-105508	19860908
	ΕP	452765				
		R: BE, CH, DE,				
	DK	8604337	Α		DK 1986-4337	19860910
	JΡ	62061919	Α	19870318	JP 1986-213704	19860910
	US	4738973	Α	19880419	US 1986-905525	19860910
	ΑU	8662601	Α	19870312	AU 1986-62601	19860911
	ΑU	588365	B2	19890914		
	CA	1273879	A1	19900911	CA 1986-518034	19860911
	US	4835151	Α	19890530	US 1987-136996	19871223
	US	4918084	Α	19900417	US 1989-323308	19890314
	US	4994475	Α	19910219	US 1989-452343	19891219
PRAI	GB	1985-22455	Α	19850911		
	GB	1986-3909	Α	19860217		
	GB	1986-3910	Α	19860217		
	US	1986-905525	A3	19860910	•	
	US	1987-136996	A3	19871223		
	US	1989-323308	A3	19890314		
os	MAI	RPAT 107:205181			•	

AB The title compds. I (R1 = OMe, OEt, OH; R2 = H, OMe, OEt, OH; R3 = Me, Et; R4, R5 = H, Me; n = 2, 3) or their pharmacol. acceptable acid addition salts are used in medications for treatment of anxiety or to counter the anxiogenic activity of benzodiazepine inverse agonists. They are also used for reduction of chronic high brain levels of serotonin or 5-hydroxyindoleacetic acid, or treatment of bacterial or viral infections. A tablet contained from I (R1 = OMe, R2 = R5 = H, R3 = R4 = Me, n = 3) (II) 100, Tranxene 10, wheat starch 7, lactose 20, and Mg stearate 1 mg. The anxiolytic activity of II in rats was between the activity of chlorodiazepoxide and diazepam, and its sedative effect was less than that of the benzodiazepines. In clin. tests the combination of II and Tranxene decreased anxiety in hospitalized depressive patients. At 120 mg/day, II stopped sleep apnea in a male patient.

IT 53873-21-5

RL: BIOL (Biological study)

Ι

(pharmaceutical, for treatment of anxiety)

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

L5 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1984:577535 CAPLUS

DN 101:177535

TI Treatment of migraine with dioxopiperidine derivatives

IN Gittos, Maurice W.; Amey, David A.

PA USA

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE ,
PI PRAI GI	US 4461771 US 1983-471099	A	19840724 19830301	US 1983-471099	19830301

$$R^{1}$$
 $R^{2}$ 
 $R^{3}N(CH_{2})n$ 
 $R^{3}$ 

AB Migraine is treated or prevented with I derivs. (R1 and R2 = H, MeO, EtO, or HO, R3 = Me or Et and n = 2 or 3) or their salts. I(R1 = MeO, R2 = H, R3 = Me, n = 3).HCl (II) [53873-28-2] was prepared by intramol.condensation of Et 4-(3-N,N-dimethylaminopropyl)-4-cyano-4-(3-methoxyphenyl)-3,3-dimethylbutanoate <math>[53873-27-1] by refluxing in 2.5N HCl. Tablets were prepared containing 50 mg II each.

IT 53873-21-5P 92519-16-9P RL: PREP (Preparation)

Ι

(preparation of, for migraine headache pharmaceuticals)

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

RN 92519-16-9 CAPLUS

CN 2,6-Piperidinedione, 3-(3,5-dimethoxyphenyl)-3-[3-(dimethylamino)propyl]-4,4-dimethyl- (CA INDEX NAME)

L5 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1975:564204 CAPLUS

DN 83:164204

OREF 83:25774h,25775a

TI Alkyl esters, dialkyl amides, and saturated heterocyclic amides of 4-aminoalkyl-4-cyano-4-phenylbutanoic and -but-2-enoic acids

IN Gittos, Maurice W.; Amey, David A.

PA Aspro-Nicholas Ltd., UK

SO Ger. Offen., 36 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2459077	A1	19750703	DE 1974-2459077	19741213
	GB 1458537	Α	19761215	GB 1973-58202	19741203
	AU 7476155	Α	19760610	AU 1974-76155	19741206
	ZA 7407769	Α	19760825	ZA 1974-7769	19741206
	US 3998965	Α	19761221	US 1974-531556	19741211
	BE 823272	A1	19750612	BE 1974-151436	19741212
	NL 7416161	Α	19750617	NL 1974-16161	19741212
	DK 7406522	Α	19750825	DK 1974-6522	19741213
	FR 2254329	A1	19750711	FR 1974-41315	19741216
	JP 50089343	Α	19750717	JP 1974-144360	19741216
	US 4035497	Α	19770712	US 1976-679165	19760422
PRAI	GB 1973-58202	Α	19731215		
	GB 1972-59761	Α	19721228		
	US 1973-425876	A2	19731218		
	US 1974-531556	A3	19741211	,	
	_ ,,	• .	1		

GI For diagram(s), see printed CA Issue.

Butenoate I, isolated as the H oxalate, was prepared by treating NaH and m-MeOC6H4CH(CN)CH2CH2NMe2 in Me2SO with PhSO2OCEt:C(CO2Et)2. Butanoic acid derivative II (R = R1 = R2 = Me, R3 = H, R4 = OEt, n = 3) (III) was prepared from m-MeOC6H4CH(CN)(CH2)3NMe2 and 3,3-dimethyl-1-ethoxyprop-2-enylidenemorpholinium tetrafluoroborate. II (R = PhCH2, Me; R1, R2 = H or Me; R3 = Me or H; R4 = morpholino, n = 2 or 3) were prepared from IV and the appropriate morpholinium tetrafluoroborate. II (R = R1 = R3 = Me, R2 = H, R4 = morpholino, n = 2) was prepared by treating Me2NCH2CH2C(CN)(C6H4OMe-m)CHMeCMe:C(OEt)R5 (R5 = morpholino) with MeSO3H and NaI in EtOH. I and III were cyclized to hydropyridines with NH3. I and II have antidepressant and cardiovascular activity (no data).

IT 53873-21-5P

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)

L5 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1974:520488 CAPLUS

DN 81:120488

OREF 81:19043a,19046a

TI Antidepressant 3-(aminoalkyl)-3-phenyl-2,6-dioxopiperidines or -tetrahydropyridines

IN Gittos, Maurice W.; Amey, David A.

PA Aspro-Nicholas Ltd.

SO Ger. Offen., 52 pp.

CODEN: GWXXBX

DT Patent LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2363052	A1	19740711	DE 1973-2363052	19731219
	DE 2363052	C2	19880721		
	AU 7363761	A	19750619	AU 1973-63761	19731218
	US 3963729	Α	19760615	US 1973-425876	19731218
•	ZA 7309598	Α	19741127	ZA 1973-9598	19731220
	BE 808958	A1	19740621	BE 1973-139144	19731221
	GB 1455687	Α	19761117	GB 1972-59761	19731227
	FR 2212147	A1	19740726	FR 1973-46908	19731228
	JP 49094683	A	19740909	JP 1974-4486	19731228
	JP 60053014	В	19851122		
	US 4035497	Α	19770712	US 1976-679165	19760422
PRAI	GB 1972-59761	А	19721228		
	GB 1973-58202	Α	19731215		
	US 1973-425876	A2	19731218		
	US 1974-531556	A3	19741211		·
CT	For diagram (a) and printed CA Tour				

GI For diagram(s), see printed CA Issue.

About 20 hydrogenated pyridines I (n = 2 or 3; R = Me2N, Et2N, or PhCH2NMe; R1 = H, 3-MeO, or 4-Cl; R2 = H, Me, or Et; R3 = H or Me; R4 = H, Me, or CO2Et) and II (R5 = Me or Et; R6 = H or CO2Et) or their salts were prepared I had antidepressant and minor parasympatholytic activity when tested i.p. in the rat. Thus, 3-MeOC6H4CH(CN)(CH2)nNMe2 (III, n = 3) was treated with NaH in Me2SO and with 4-(1-ethoxy-3,3-dimethyl-2-propenylidene)morpholinium tetrafluoroborate to give 3-MeOC6H4C(CN)[(CH2)3NMe2]CMe2CH:CR7 - OEt (R7 = morpholino), which was cyclized in H2SO4 and AcOH at 100° to give I (n = 3, R = Me2N, R1 = 3-MeO, R2 = R3 = Me, R4 = H). III (n = 2) was treated with NaH in Me2SO and with PhSO3CEt:C(CO2Et)2 to give 3-MeOC6H4C(CN) (CH2CH2NMe2)CEt:C(CO2Et)2, which on treatment with H2SO4 and AcOH at 100° gave II (R5 = Et, R6 = CO2Et).

IT 53873-21-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 53873-21-5 CAPLUS

CN 2,6-Piperidinedione, 3-[3-(dimethylamino)propyl]-3-(3-methoxyphenyl)-4,4-dimethyl- (CA INDEX NAME)